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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| SCHWADRON, RONALD B | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/577,167 | BRISCOE ET AL. | |
| | Examiner | Art Unit | |
| | Ron Schwadron, Ph.D. | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,9,11,13,15,17,30-32 and 34-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,11,13,15,17,30-32,34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The ADS is defective because Inventor Reinders name is listed differently in the oath than in the ADS. A new ADS is required.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-7,9,11,13,15,30,31,34,37,38,39 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants arguments have been considered and deemed not persuasive.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed methods.

The claims encompass use of a VEGF antagonist or an antibody against VEGF as an antagonist or the generic antagonists of claim 34. Regarding use of antibody against human VEGF, it appears that human VEGF of specific amino acid sequences were known in the art. However, the claims encompass use of antibody which binds unknown variants or alleles of human VEGF wherein the identity of said unknown variants or alleles of VEGF are unpredictable. Regarding use of VEGF antagonists per se, said antagonists encompass a vast collection of unknown agents wherein the identity of said molecules is unpredictable. Whilst the specification discloses specific examples of VEGF antagonists, the claims encompasses use of any agent that is a VEGF antagonist and wherein the identity of said agent is not known or

predictable based on known antagonists (for example the molecules recited in claim 34). For example whilst several small molecule inhibitors are recited in claim 36, the term encompasses a plethora of unknown molecules that are structurally unrelated to the specific molecules recited in claim 36 and wherein the identity of such molecules is unpredictable. Thus, the written description provided in the specification is not commensurate with the scope of the claimed inventions. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the

mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the
sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

Regarding applicants comments, the claims encompass use of antibody which binds unknown variants or alleles of human VEGF wherein the identity of said unknown variants or alleles of human VEGF are unpredictable. The only claim which recites a VEGF sequence is claim 40. Regarding applicants comments about screening methods, attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.
Regarding applicants comments, it is irrelevant that the claims are drawn to a method that uses the aforementioned reagents versus the reagents themselves.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-4,6,7,9,11,34,36,38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Armstrong et al. (US Patent 5,547,959). Applicants arguments have been considered and deemed not persuasive

Armstrong et al. discloses pretransplantation treatment of the allograft

donor graft and recipient with parentally administered rapamycin ( a VEGF antagonist as per claim 36) to treat graft rejection (see columns 2-4, especially column 3, third paragraph). Armstrong et al. discloses that the immunosuppressive agents CSA or FK-506 or prednisone can be used in combination with said treatment (see column 4). The graft can be a heart allograft (see columns 3-4).

Regarding applicants comments, Armstrong et al., column 3, third paragraph teaches:

"***Parenteral*** **administration of immunosuppressant agents such as cyclosporin A, cyclophosphamide, methylprednisone, FK506, or rapamycin to a tissue or organ *donor* before transplant has been shown to reduce rejection of the transplanted tissue or organ.**".

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-7,9,11,15,30,31,34,36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armstrong et al. (US Patent 5,547,959) in view of Feldmann et al. (WO 98/51344). Applicants arguments have been considered and deemed not persuasive.

Armstrong et al. discloses pretransplantation treatment of the allograft donor graft and recipient with parental rapamycin ( a VEGF antagonist as per claim 36) to treat graft rejection (see columns 2-4, especially Colum 3, third paragraph). Armstrong et al. discloses that the immunosuppressive agents CSA or FK-506 or prednisone can be used in combination with said treatment (see column 4). The graft can be a heart allograft (see columns 3-4). Armstrong et al. do not disclose use of the antibody recited in the claims or use of a kidney graft or method of claim 39. A routineer would have used routine experimentation to determine the optimal time of donor treatment. Feldmann et al. discloses the treatment of kidney allograft rejection using a VEGF antagonist such as a humanized antibody or polyclonal against VEGF (see page 6, 7, 29 and claims 29-34). Polyclonal antibodies against VEGF would bind all epitopes on said molecule including those present in the antibody of claim 40. Feldmann et al. disclose that the amount and schedule of administration of VEGF inhibitor antibody would be determined by routine experimentation and could be given for multiple days depending on the desired effect (see page 36). Armstrong et al. teach that the rapamycin can be coadministered with another agent that treats allograft rejection (see column 4, third paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the antiVEGF antibody to the recipient receiving the rapamycin treated graft and to the graft donor because Armstrong et al. discloses treatment of the allograft donor graft and recipient with rapamycin to treat graft rejection and that other immunosuppressive agents can be used in combination with said treatment and a routineer would have used routine experimentation to determine the optimal time of donor treatment whilst Feldmann et al. discloses the treatment of kidney allograft rejection using a humanized antibody against VEGF antibody or polyclonal against VEGF wherein said antibodies against VEGF would bind all epitopes on said molecule including those present in the antibody of claim 40 and Feldmann et al. disclose that the amount and schedule of administration of VEGF inhibitor antibody would be determined by routine experimentation and could be given for multiple days depending on the desired effect. The method could have been used with any graft donor and could have been used to treat kidney graft donors/rejection as per taught above by

Feldmann et al. One of ordinary skill in the art would have been motivated to do the aforementioned because Armstrong et al. discloses treatment of the allograft donor graft and recipient with rapamycin to treat graft rejection and that other immunosuppressive agents can be used in combination with said treatment whilst Feldmann et al. discloses the treatment of kidney allograft rejection using a humanized antibody or polyclonal antibody against VEGF.

Regarding applicants comments, Armstrong et al., column 3, third paragraph teaches:

"***Parenteral*** **administration of immunosuppressant agents such as cyclosporin A, cyclophosphamide, methylprednisone, FK506, or rapamycin to a tissue or organ *donor* before transplant has been shown to reduce rejection of the transplanted tissue or organ.**".

8. Claims 17/32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armstrong et al. (US Patent 5,547,959) in view of Feldmann et al. (WO 98/51344)as applied to claims 1-7,9,11,15,30,31,34,36-40 above, and further in view of Cutler et al. (US 2003/0185831).

The previous rejection renders obvious the claimed invention except for use of Bevacizumab. Feldmann et al. discloses the treatment of kidney allograft rejection using a humanized antibody against VEGF. Bevacizumab is an art known antibody inhibitor of VEGF (see Cutler et al., [0306]). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use of Bevacizumab, Feldmann et al. discloses the treatment of kidney allograft rejection using a humanized antibody against VEGF and Bevacizumab is an art known antibody against VEGF.

Regarding applicants comments, Armstrong et al., column 3, third paragraph teaches:

"***Parenteral*** **administration of immunosuppressant agents such as cyclosporin A, cyclophosphamide, methylprednisone, FK506, or rapamycin to a tissue or organ *donor* before transplant has been shown to reduce rejection of the transplanted tissue or organ.**".

9. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Armstrong et al. (US Patent 5,547,959) in view of Feldmann et al. (WO 98/51344)as applied to claims 1-7,9,11,15,30,31,34,36-40 above, and further in view of Wood et al. (US 2006/0270665).

The previous rejection renders obvious the claimed invention except for use of PTK787. Feldmann et al. discloses the treatment of kidney allograft rejection using a VEGF antagonist. PTK787 is an art known VEGF antagonist (see Wood et al., [0062]) wherein Feldmann et al. indicates that VEGF antagonist encompasses VEGF receptor inhibitors (see page 28, first complete paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use PTK787, Feldmann et al. discloses the treatment of kidney allograft rejection using a VEGF antagonist, whilst PTK787 is an art known VEGF antagonist.

Regarding applicants comments, Armstrong et al., column 3, third paragraph teaches:

"***Parenteral*** **administration of immunosuppressant agents such as cyclosporin A, cyclophosphamide, methylprednisone, FK506, or rapamycin to a tissue or organ *donor* before transplant has been shown to reduce rejection of the transplanted tissue or organ.**".

10. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Armstrong et al. (US Patent 5,547,959) in view of Feldmann et al. (WO 98/51344)as applied to claims 1-7,9,11,15,30,31,34,36-38,40 above, and further in view of Neville et al. (US 2005/0142117).

The previous rejection renders obvious the claimed invention except for use of MMF.. Armstrong et al. discloses that additional immunosuppressive agents can be used in combination with said treatment (see column 4). Neville et al. teach the art known immunosuppressive agent MMF (mycophenolate mofetil)(see [0032] and [0077]).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the

previous rejection renders obvious the claimed invention except for use of MMF whilst Armstrong et al. discloses that additional immunosuppressive agents can be used in combination with said treatment (see column 4) and Neville et al. teach the art known immunosuppressive agent MMF (mycophenolate mofetil)

Regarding applicants comments, Armstrong et al., column 3, third paragraph teaches:

"***Parenteral*** **administration of immunosuppressant agents such as cyclosporin A, cyclophosphamide, methylprednisone, FK506, or rapamycin to a tissue or organ *donor* before transplant has been shown to reduce rejection of the transplanted tissue or organ.**".

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571 272-0735. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
Ron Schwadron, Ph.D.
Primary Examiner, Art Unit 1644